



Corporate Headquarters

4/12/99

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Dockets Management Branch HFA-305  
Food & Drug Administration  
5630 Fishers Lane  
Rockville, MD 20852

**RE: Docket # 98D 0785**  
**Draft Guidance for Industry: Developing Medical Imaging Drugs & Biologics**

Dear Sir/Madam:

We are pleased to have the opportunity to comment on this draft guidance released by FDA. The following comments are offered.

**Section I Introduction (page 1)**

The guidance discusses "potential claims for medical imaging drugs and the nature of promotional materials for such claims." Discussion of promotional materials also occurs frequently in the guidance. We feel that discussion of promotional claims should be eliminated from the guidance. Promotional claims are dependent upon the nature of the data that is collected and presented in the NDA. The proposed guidance appears to limit promotional claims to the information contained in the approved indication. Is it the position of the agency that only information that is contained in the package insert for a Medical Imaging Drug Product may be used in promotional materials? Valid efficacy information contained in the NDA which are relevant to the approved indication should be allowed in promotional claims. We would suggest deleting references to promotional claims and replacing statements regarding "potential claims" with "potential indications" in the guidance.

**Section III D Diagnostic or Therapeutic Patient Management (page 7)**

It should be recognized that it may not be appropriate to ask a clinical trial investigator if an investigational new drug in a clinical study had an effect on patient management or clinical outcomes. Often questions on case report forms may be worded hypothetically such as; "Could the information provided by the use of x change this patient's management or treatment." The guidance should clarify the use of responses to questions of this type in establishing the drug's efficacy.

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**Section IV (page 8)**

The guidance states that "To establish a claim for a medical imaging drug, a sponsor should characterize the drug's clinical usefulness and demonstrate that the information provided is valid and reliable. Clinical studies should be performed in defined clinical settings." The clinical usefulness in a defined clinical setting of a medical imaging drug product is best determined by the efficacy evaluations conducted by the clinical trial investigator. At the public meeting on March 26, 1999 it was noted that the agency reviews efficacy data obtained from clinical sites and compares it with blind read results. If a sponsor prospectively states that this data will be used for the efficacy determination of the drug and the data is adequately identified as coming from an unblinded evaluation conducted by the clinical trial investigator, then this data should be permitted inclusion in product labeling and in fairly balanced (with blind read data) promotional claims.

**Section IV D**

This comment pertains to part 1 b, paragraph 2 (page 12) and part 2, paragraph 3 (page 13) of the above section.

The guidance recommends that studies should generally include subjects that adequately represent the "spectra of normality and abnormality". Patient recruitment is often difficult in clinical trials and requiring enrollment of sufficient patients representing the "spectra of normality and abnormality" is a burden that may unduly prolong or expand clinical trials or result in broad indications being impossible to attain. We would suggest that other data may be used to support studies including data on the mechanism of action of the drug product and information from the literature, including medical text books, regarding the effect of other illnesses, processes and diseases on the potential use of the drug.

**Section VIII Part A 1 (page 23)**

The guidance states the "spectrum of other conditions, processes, or diseases that may confound interpretation of the results for the disease or condition of interest also should be appropriately represented." As noted previously patient recruitment is often difficult in clinical trials and requiring enrollment of sufficient patients representing the full spectra of conditions, processes, or diseases that may confound interpretation of the results of a diagnostic study is a burden that may unduly prolong and expand clinical trials or result in broad indications being impossible to attain. We would suggest that other data may be used to support studies such as data on the mechanism of action of the drug product and information from the literature, including medical text books, regarding the effect of other conditions, processes and diseases on the potential use of the drug.

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**Section VIII B 1 Characteristics of the Readers**  
Paragraph 2 of the above section (page 25)

The guidance states that an *Independent Reader* is one who is "not otherwise affiliated with ..... institutions at which the studies are conducted." We strongly object to the notion that simply because a physician may be affiliated with an institution, that this affiliation (or employment) means the individual is biased and cannot be an independent reader. This exclusion would apply even if the physician in question had never seen the study protocol, had never heard of the test drug or was in a different department or perhaps even in a different affiliated hospital. Such a physician would be disqualified from being an independent reader. This restriction is arbitrary and will unnecessarily prevent qualified physicians from participating in blind read studies. It should be deleted.

Paragraph 4 of the above section (page 26):

We would suggest adding to this section examples of types of information that could be presented to a blinded reader. Such information may include: institution conducting the study, imaging parameters, equipment data, and subject demographic information.

Paragraph 5 of the above section (page 26):

We support the concept of a prospectively designed "fully informed blind read" which was discussed during the public meeting held on March 26, 1999. It should be possible to provide a blind reader with information regarding patient demographics, imaging parameters and equipment, patient medical history including the results of non-imaging tests and the anatomical region being evaluated. This reading would be more reflective of the clinical setting for the use of the contrast agent and the data provided would be more clinically useful than a completely blinded reading of images. Readers in these studies would still be blinded to the final diagnosis as well as identification of the test drug or comparator used to generate the image.

**VIII D 2 Placebos**

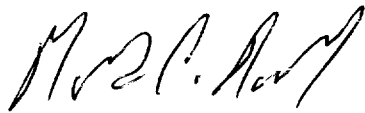
We agree that use of a placebo may be helpful in an assessment of the safety of a contrast agent. Adverse events may be caused due to the anxiety of the patient or due to the imaging procedure itself. Adverse events with placebos may be used as an aid to understanding the true safety profile of a medical imaging drug product. The guidance should state that if safety data is collected with placebos in controlled clinical studies then this data should be permitted to be described in the package insert.

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It is noted in the guidance that some placebos used in diagnostic studies can have diagnostic effects. It should also be noted that if a placebo does not have a diagnostic effect it should not be required to be used in a determination of the efficacy of the medical imaging drug. In such cases placebos are not needed to evaluate efficacy as the pre-contrast images would be expected to appear the same as images taken with placebos.

Thank you for the opportunity to comment on this draft guidance.

Sincerely,

A handwritten signature in black ink, appearing to read 'Mark C. Roessel', with a stylized flourish at the end.

Mark C. Roessel  
Vice President Regulatory Affairs  
C:regulatory/midguide

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